



**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: Charych, et al.

Attorney Docket No.: CHIRP014

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Application No.: 09/874,091

Examiner: Tran, My-Chau T.

APR 06 2005

Filed: June 4, 2001

Group: 1641

Title: MICROARRAYS FOR PERFORMING  
PROTEOMIC ANALYSES

**DECLARATION UNDER 37 CFR § 1.132**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Deborah Charych, declare as follows:

1. I am a co-inventor of the above-identified patent application.
2. I earned a Ph.D. in Physical / Analytical Chemistry from the University of California, Berkeley in 1992. I currently serve as Vice-Chairman of the Board of Trustees for the Gordon Research Conferences and Chairman of the Gordon Research Conference, Chemical Sensors and Interfacial Design section. I am a co-inventor on six issued U.S. patents and more than a dozen pending U.S. patent applications, and a coauthor of over 20 published papers in the fields of combinatorial chemistry, genomics and proteomics microarrays, and biomaterials.
3. I was a Principal Investigator and Program Manager in the Biomolecular Materials Program, Lawrence Berkeley National Laboratory, Berkeley, CA from 1993-1998. Since 1998, I have worked as a research scientist at Chiron Corporation, Emeryville, CA (hereinafter "Chiron"), where I currently hold the position of Senior Scientist, Proteomic and Genomic Expression Technologies/Bioorganic Chemistry.
4. My work at Chiron has focused on the development of new combinatorial synthetic methods and genomic and proteomic techniques and materials, including microarray experimental design and materials development.

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5. The application presently claims an aspect of the invention directed to an array of protein-binding agents stably attached to the surface of a solid support, the array comprising a solid substrate having a substantially planar surface comprising a layer of aluminum formed on a glass base material, the aluminum coated with a silicon dioxide coating having a thickness of between about 200 and 900 Å. The claimed range of silicon dioxide thickness is a critical feature of the invention presently claimed since we have found that this thickness provided optimal amplification of a fluorescent signal from a labeled protein bound to the array.
6. I have reviewed the references cited against the present application, in particular US Patent No. 5,478,527 to Gustafson et al. ("Gustafson"). Gustafson is directed to an entirely different type of array and assay technology that, with particularly relevance, does even not involve labeled proteins. Rather, Gustafson is specifically addressed to providing a suitable substrate for its reflective diffraction biograting. In various embodiments, Gustafson describes substrates composed of silicon applied over silicon dioxide (e.g., see Fig. 4) and in which silicon dioxide is applied over a reflective metal deposited on silicon. The objective is to provide an optically flat reflective substrate that apparently enhances reflective diffraction from a biograting formed on the substrate. Since Gustafson's substrate is specifically designed for their biograting immunoassay, and this assay is label free (i.e., it does not make use of fluorescently labeled probes), it is my judgment that a skilled worker in this field at the time that our invention was made would not have been led to our invention by Gustafson in combination with the other cited references. I do not believe that a person skilled in the art would have seen any advantage in combining the teachings of Gustafson and the other references to which the Examiner has referred, namely Pease, Wagner and Barrett, since Gustafson's teaching of the use of a flat substrate of silicon dioxide on reflective metal would have been viewed as specific to their particular label-free assay.
7. More specifically, with regard to the array substrate disclosed by Gustafson, the reference provides no teaching with regard to a suitable array substrate for a fluorescence-based assay, and certainly not for optimization of such an array substrate, as claimed. In experiments conducted by me or under my direction at Chiron, the fluorescent signal obtained from a labeled protein bound to an array having various thicknesses of silicon dioxide and otherwise constructed as claimed was tested. At oxide thicknesses below 200 Å (e.g., thicknesses of about 110 to 140 Å) no signal was detected. The signal obtained from arrays having silicon dioxide thicknesses in the 1200-1300 Å range was poor. Intermediate silicon dioxide thicknesses, however, i.e., greater than 200 Å and in particular about 800-900 Å

